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## Accepted Manuscript

Title: Lung cancer mortality in Australia: Projected outcomes to 2040

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# Lung cancer mortality in Australia: Projected outcomes to 2040

**Short title:** Lung cancer mortality in Australia

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### Highlights

- Validated a statistical model to project lung cancer mortality rates to 2040.
- Lung cancer mortality rates are expected to continually decline in Australia.
- Number of lung cancer deaths will continue to be substantial and to increase.
- These results will inform planning to meet future health service needs.
- Projected rates can serve as a benchmark for tobacco control in Australia.

## **Abstract**

### **Objectives**

The aim was to develop and validate a statistical model which uses past trends for lung cancer mortality and historical and current data on tobacco consumption to project lung cancer mortality rates into the future for Australia.

### **Methods**

We used generalized linear models (GLMs) with Poisson distribution including either age, birth cohort or period, and/or various measures of population tobacco exposure (considering cross-sectional smoking prevalence, cigarettes smoked and tar exposure per capita). Sex-specific models were fitted to data for 1956-2015 and age-standardized lung cancer mortality rates were projected forward to 2040. Possible lags of 20-30 years between tobacco exposure and lung cancer mortality were examined. The best model was selected using analysis of deviance. To validate the selected model, we temporarily re-fitted it to data for 1956-1990 and compared the projected rates to 2015 with the observed rates for 1991-2015.

### **Results**

The best fitting model used information on age, birth cohort and tar exposure per capita; close concordance with the observed data was achieved in the validation. The forward projections for lung cancer mortality using this model indicate that male and female age-standardized rates will decline over the period 2011-2015 to 2036-2040 from 27.2 to 15.1 per 100,000, and 15.8 to 11.8 per 100,000, respectively. However, due to population growth and ageing the number of deaths will increase by 7.9% for males and 57.9% for females; from 41,040 (24,831 males, 16,209 females) in 2011-2015 to 52,403 (26,805 males, 25,598 females) in 2036-2040.

## Conclusion

In the context of the mature tobacco epidemic with past peaks in tobacco consumption for both males and females, lung cancer mortality rates are expected to continually decline over the next 25 years. However, the number of lung cancer deaths will continue to be substantial, and to increase, in Australia's ageing population.

**Keywords:** lung cancer mortality; statistical projections; Australia; tobacco consumption; generalized linear models; cohort effect; population-based; health service planning; tobacco epidemic

## 1. Introduction

Lung cancer has been the most common cause of cancer death over the last five decades in Australia[1]. Evidence of a strong causal association between tobacco smoking and lung cancer has been well established since the early 1950s [2]. Australia has successfully implemented many tobacco control interventions, and there have been subsequent reductions in lung cancer mortality [3]. However, despite the marked decline in smoking prevalence seen for Australian males since the 1950s and Australian females since the 1980s [3], it is still estimated that lung cancer will be the largest cause of cancer death in 2017 [4].

Cancer mortality is an important measure of the burden of cancer in a population, and can be of great use in informing the planning of health services and resource management [5, 6]. As tobacco exposure is the most significant risk factor for lung cancer [2], it is well accepted that it is an important explanatory factor for lung cancer mortality [6, 7]. The projected impact of tobacco control policies on future lung cancer mortality rates is crucial to understanding the success of such policies [5, 7]. However, lung cancer mortality projections have commonly been based solely on past mortality trends, due to the scarcity of data on historical smoking behaviour at the population level [8]. Currently, the most common method for projecting cancer incidence and mortality is to use age-period-cohort (APC) models. The basis of APC models is well explained in the published literature [9, 10], but in brief, APC models describe the rate of an event as a function of age, period and cohort effects. There is, however, a non-identifiability problem inherent in APC models due to the linear relationship between age, period and cohort [9]. While there have been some developments in methods to overcome the non-identifiability problem [10-16], there is no way to distinguish the period effect and the cohort effect, and the parameter estimates

obtained can be sensitive to the choice of constraints placed on the period and cohort factors [6, 17].

Some previous studies have reported the inclusion of detailed smoking data as a factor in lung cancer mortality projections [6, 7, 18, 19]. Brown and Kessler (1988)[6] using data for the United States of America (USA) and Shibuya et al., (2005)[7] using data for Australia, USA, United Kingdom and Canada, fitted a Generalized Linear Model (GLM) using Poisson regression for lung cancer mortality rates with terms for age, cohort and lagged sex-period-specific cigarette tar consumption [6, 7]. One other study by Preston et al. (2014) used a log-linear binomial regression model for lung cancer mortality rates in the USA with terms for age and number of years of smoking prior to age 40 [18], and a study using Spanish data by Martin-Sanchez et al., (2017) used a linear regression model to predict lung cancer mortality rates based on smoking prevalence for two large age groups [19]. Here, we propose an alternative model to project lung cancer mortality rates using GLMs with a Poisson distribution including age and cohort, or age and period, together with sex-age-cohort-specific smoking-related variables. As with the methods used by Brown and Kessler (1988) [6], Shibuya et al. (2005) [7], and Preston et al. (2014) [18], our model does not suffer the non-identifiability problem. With this model, we are also able to examine the period or cohort effect after adjusting for smoking-related variables.

Due to delays in the impact of changes in smoking behaviour, lung cancer mortality rates to 2040 are expected to predominantly reflect tobacco exposure that has already occurred. The aim of this study was therefore to develop and validate a statistical model to project age-standardized lung cancer mortality rates and numbers of deaths from lung cancer for



the period 2016 to 2040, based on past trends in lung cancer mortality and historical and current data on tobacco consumption for the Australian population.

## **2. Material and Methods**

### **2.1. Data sources**

#### **2.1.1 Lung cancer mortality and population data**

We obtained from the World Health Organization (WHO) Mortality Database (MDB) [20], national tabulated data on the numbers of deaths from lung cancer in Australia by sex, age and calendar year from 1956 to 2015 to allow for a minimum of 20 years of observed data before the peak in lung cancer mortality rates for males was reached in the early 1980s. The data available in the WHO MDB comprise deaths registered in national vital registration systems with underlying cause of death as coded by the relevant national authority in each country. Australia is one of the countries with near complete population coverage [20]. In Australia, it is a legal requirement for each state and territory to record all deaths in registries administered by the various state and territory Registrars of Births, Deaths and Marriages, and either a medical practitioner or a coroner is required to certify the cause of death [21]. The corresponding Australian population data by sex, 5-year age group and calendar year from 1956 to 2040 were obtained from the Australian Historical Population Statistics and Population Projections (Series B, based on medium population growth) produced by the Australian Bureau of Statistics (ABS) [22, 23]. For the purposes of our analyses, we grouped the mortality data into 5-year age groups and 5-year periods. Deaths from lung cancer that occurred before the age of 30 were excluded, as death from lung cancer is rare for this age group [1].

### 2.1.2. Data on smoking patterns in Australia

We obtained the data on smoking from two data sources: the International Smoking Statistics (ISS) Web Edition [24], and the National Drug Strategy Household Surveys (NDSHS) for 2007-2016 [25-28]. Integrated ISS and newly released NDSHS data are hereafter referred to as “ISS-NDSHS data”. As data on smoking behaviour for pre-adolescents and young adolescents is very scarce, and is not included in the sales adjustment calculations in the ISS, we did not include smoking information for those under 15 years of age. Although smoking clearly does occur below this age, it is at a much lower level than for the adult population [25-28].

#### *ISS data*

The ISS database provides data from different surveys, and provides information on annual tobacco sales from 1920 to 2010, smoking prevalence by age group and sex from 1945 to 2004, and number of cigarettes consumed per person per day by age group and sex from 1972 to 2004 [24]. Data for men and women from nationally representative surveys were separately included. When multiple surveys were available, *a priori* defined selection criteria (as described in Appendix 1) were applied to determine which data sources to include in the current analysis for each calendar year.

#### *NDSHS data*

The NDSHS is one of the national surveys included in the ISS up to 2004, and has been conducted at three yearly intervals since 1985 [24]. The newly released NDSHS data for 2007- 2016 were processed using the same methods previously described for the ISS data [24] to extend the smoking prevalence and tobacco consumption data to 2016. The

Absolute Person Weight was used in the calculation of the smoking statistics to ensure that the sample is representative of the population [27].

## **2.2. Outcome and study variables**

The outcomes of interest were the lung cancer mortality rate and the number of deaths from lung cancer by 5-year calendar period for men and women. Study variables used in this analysis included sex, 5-year age group, 5-year calendar period and 5-year birth cohorts, which were coded as the middle year of each five year period. Person-years at risk were approximated by the population estimates for the middle year of the five year period [6]. Several smoking-related variables were considered, including the smoking prevalence, number of cigarettes sold, number of cigarettes consumed per capita, and average tar per cigarette. Previous research has suggested that there is a considerable lag between the initiation of smoking and the development of lung cancer [29], but that this lag may vary considerably across populations and countries [6, 7, 30-33]. In this study, all sex-specific smoking-related variables were lagged by 20-30 years in each model for males and females separately. In order to allow for a 30-year lag, all smoking-related variables were reconstructed backwards to 1930 and projected forwards to 2020, and were aggregated into 5-year periods. Similar backward reconstruction techniques were used by Adair et al. and Shibuya et al. to estimate tobacco consumption data [3, 7]. The data sources and the estimation process for each smoking-related variable are summarised and described in detail in Appendix 2.

## **2.3. Statistical analyses**

Given the inherent non-identifiability problem in APC models due to the linear relationship between age, period and cohort [9], additional strategies are required to deal with this, and so these models need to be implemented using special software packages which often don't allow the user to modify the prediction of future cohort and period effects. We therefore chose to use GLMs with a Poisson distribution including age, birth cohort and smoking-related variables, or age, period and one or more different smoking-related variables.

Possible lags of 20-30 years between cigarette tar exposure and lung cancer mortality were examined for each GLM fitted model. To assess the best model for each sex with different smoking-related variable(s), we compared the fit of various models to data for 1956-2015 using analysis of deviance [6, 34]. The best fitting model was selected on the basis of minimising the deviance as a measure of goodness-of-fit [6], and the best smoking-related variable to predict lung cancer mortality was found to be the sex-age-specific cigarette tar exposure with a lag of 26 years for males and 29 years for females. Consistent with previous studies, we confirmed that the cohort effect is a stronger predictor than the period effect for lung cancer mortality projections, as cohort effects reflect changes in early life exposure to risk factors such as smoking [6, 7, 35]. Our final model can be presented as a parsimonious equation:

$$\ln D_{ij} = \ln N_{ij} + \alpha \text{Age}_i + \beta \text{CTC}_{ij-L} + \gamma \text{Cohort}_{l-i+j} + \varepsilon_{ij}$$

where  $D_{ij}$  and  $N_{ij}$  denote the number of deaths from lung cancer and the number at risk in the population for the  $i^{\text{th}}$  age group during  $j^{\text{th}}$  calendar period;  $\text{Age}_i$  denotes the age group 30-34, 35-39, ...,  $\geq 85$  years, and  $\text{Cohort}_{l-i+j}$  denotes the birth cohorts 1875-1879, 1880-1884, ..., 1980-1984;  $\text{CTC}_{ij-L}$  denotes the cigarette tar exposure for the population in the  $i^{\text{th}}$  age group during  $j-L^{\text{th}}$  calendar period, which is lagged by  $L$  years (26 years for males and 29

years for females). The characteristics of different models using standard GLMs are summarized in Appendix 3.

To validate the selected projection model, we fitted the model to the data for 1956-1990 and then projected forward to 2015. We then compared the predicted lung cancer mortality from the model for the period 1991-2015 with the actual observed data for the period. Confidence intervals and statistical significance of standardized mortality rate ratios of the observed and predicted mortality rates were calculated using formulae from Boyle and Parkin [36]. Comparisons of our final model with an age-cohort model and age-cigarette tar exposure model which excluded a cohort effect, fitted using the standard GLM, are shown in Appendix 4. We also compared these models with an APC model fitted by the `apcspline` command in Stata 13 [13] with natural cubic splines for smoothing. Details of the methods used by the `apcspline` command are provided elsewhere [13]. Briefly, we compared a number of APC models with different numbers of knots for the age, period and cohort effects to identify the one with the lowest Bayesian information criterion (BIC). We applied a default damping factor (0.92) to the drift when projecting rates to the future, and future period and cohort effects were assumed to be the same as those for the most recent observed period and cohort [13].

To project lung cancer mortality beyond the observed calendar period, we assumed that the age effect remained unchanged over time and reflects the general level of lung cancer risk in the non-smoking population [6, 7]. The cohort effect is considered to be a reflection of many cohort-specific smoking characteristics, but unfortunately not all were available for this study. We tested the variation in the cohort parameters explained by each cohort-

specific smoking characteristic using linear regression. We found that cohort-specific cigarette tar exposure was the best predictor for the cohort effects compared to the other smoking-related variables considered for inclusion in the model, and so we used cigarette tar exposure per capita to estimate future cohort parameters. We also assumed that other relevant factors which can be attributed to period effects will remain constant over time, such as environmental, occupational, cancer diagnosis and treatment factors. All age-standardized lung cancer mortality rates presented in this paper were standardized to the WHO World Standard Population [37].

We also conducted sensitivity analyses by fitting the projection models under the assumption that there had been no change in tar content since 1995 and also by using different backwards estimated cigarette consumption data. A parametric bootstrap simulation technique was used to compute 95% prediction intervals for model coefficients. All statistical analyses were performed using Stata (version 13.1, STATA Corporation, College Station, TX).

### **3. Results**

Figure 1 shows smoking prevalence, the annual number of cigarettes smoked per capita, and annual cigarette tar exposure (g) per capita by sex and calendar period for the Australian population aged 15 years or above. For males, the smoking prevalence has decreased since around the 1950s, prior to which rates were fairly stable from around 1930. The other measures of exposure, the number of cigarettes smoked per capita and the annual tar exposure per capita, have been declining from peaks in the early 1960s and late 1950s, respectively, after prior increasing trends. The trend for females in both smoking

prevalence and number of cigarettes smoked has been one of gradual increase towards their peaks around the 1980s which were later than for males, followed thereafter by a decline. Unlike the other two exposure variables, the decline in cigarette tar exposure per capita for females is similar in timing to that for males, but at a much slower pace until the mid-1980s. In the past, females had lower exposure according to all measures compared to males in the same calendar year, but projected values show that the exposure by sex, for each measure, is expected to converge around the year 2020. Given the significant reduction in both tobacco consumption and average tar content of cigarettes (which between 1980 and 1994 dropped from 13.2 to 6.4 mg per cigarette, and is estimated to have reached 5.3 mg per cigarette in 2000), for both males and females, the decline in cigarette tar exposure (Figure 1 C) occurred at a much faster pace than for the other two measures (Figure 1 A and B) and reached very low levels in the early 2000s.

Figure 2 shows the smoking prevalence, the number of cigarettes smoked and tar exposure by birth cohort and age. For males, the overall peak in number of cigarettes smoked and cigarette tar exposure occurred at age 35-45 for cohorts born in the 1910s and 1930s and the prevalence of smoking was also greatest for earlier birth cohorts (back to the 1900s), while for females the overall peaks in number of cigarettes smoked and smoking prevalence appear to occur at a younger age (25-40 years) for more recent cohorts, born around the 1950s to 1970s, but the peak in cigarette tar exposure appears to have occurred for earlier cohorts at older age (35-45 years).

The 25-year validation of the final models was based on the observed mortality data from 1956 to 1990 with cigarette tar exposure data lagged by 26 years for males and 29 years for

females, projected to 2015. Figure 3 shows the comparison of the predicted and observed age-standardized lung cancer mortality rates in 1991-2015. The fitted rates for 1956-1990 and the projected rates for 1991-2015 for both males and females are close to the observed values, with no significant differences observed, suggesting that the model appears to provide valid projections of lung cancer mortality in Australia. The sensitivity analyses that were conducted by applying constant average tar content per cigarette for 1994 into the future and using different backwards estimated cigarette consumption data resulted in minimal change to the projection models (data not shown).

The estimated age and cohort effects and the regression coefficient for cigarette tar exposure are shown in Appendix 5. There are strong and significant associations between the lung cancer mortality rate and all three of age, cohort, and lagged tar exposure. The slope of the sex-age-specific tar exposure differs by sex, with a larger slope for females than for males (estimated coefficient for males: 0.0032, 95% CI: 0.0028-0.0036; for females: 0.0062, 95% CI: 0.0053-0.0072). After adjusting for lagged cigarette tar exposure and age, male lung cancer mortality peaked for the cohorts born around the 1910s to 1930s, while the female mortality rate peaked for the cohorts born around the 1940s to 1960s.

The observed and predicted age-specific mortality rates are presented in Figure 4 and the observed and predicted numbers of deaths from lung cancer and age-standardized lung cancer mortality rates are presented in Table 1 and in Figure 5. Both male and female age-standardized rates are projected to decline over the period 2011-15 to 2036-2040 from 27.2 to 15.1 per 100,000, and 15.8 to 11.8 per 100,000, respectively. For both males and females, the lung cancer mortality rate is consistently low for those aged under 55 years. The



mortality rates for all age groups above 54 years declined steadily for males since the 1980s. By contrast, for females, a slow decrease in mortality rates was only observed for the 55-64 and 65-74 years age groups after the 2010s. The mortality rate for females aged  $\geq 75$  levelled off after 2010 and is predicted to continue at the same level to 2040. Due to population growth and ageing the number of deaths will increase by 7.9% for males and 57.9% for females; from 41,040 (24,831 males and 16,209 females) in 2011-2015 to 52,403 (26,805 males and 25,598 females) in 2036-2040.

#### **4. Discussion**

We have developed and validated a flexible model in which predicted future lung cancer mortality is a function of age, birth cohort and sex-age-specific per capita cigarette tar exposure in the Australian population. Projections for lung cancer mortality based on this model indicate that a decreasing trend in the male mortality rate will continue to 2040, and that the female mortality rate peaked in 2010. However, the numbers of deaths due to lung cancer will increase to 2040, driven by population growth and ageing. Age, birth cohort and cigarette tar exposure were found to be the strongest predictors for future lung cancer mortality, and the effect of birth cohort and the lag in years between cigarette tar exposure and lung cancer mortality appear to differ by sex. Our best-fitting model assumed a lag of 26 years for males and 29 years for females between tobacco exposure (as measured by population average per capita tar exposure) and lung cancer mortality. Unfortunately, this considerable lag implies that lung cancer mortality rates in the intermediate term (to 2040), cannot be substantially altered via further current initiatives in tobacco control alone, although it is very important to note that the benefits of current and new tobacco control

policies will be manifest thereafter (estimating these benefits are the subject of our future work).

There have been a few previous international studies that have reported statistical projection models for lung cancer mortality incorporating smoking-related factors as one of the covariates [6, 7, 18, 19, 31]. Only one study (Shibuya et al., 2005) reported long term projections of lung cancer mortality using data for the Australian population [7]. Similar to the model developed by Brown and Kessler [6], Shibuya and colleagues [7] used GLMs with lung cancer mortality data up to 1999 and projected to 2035, and the model was validated by excluding the five most recent years of data from the model fitting and comparing the predicted rates with those observed. Shibuya et al.'s model was a function of sex-period-specific cigarette tar exposure. In our model, we identified sex-age-cohort-specific cigarette tar exposure as the best predictor among the available smoking-related variables. Our study confirmed a significant association between cigarette tar exposure and lung cancer mortality rates, and the overall mortality trends were consistent with the projections reported by Shibuya et al., with particularly good agreement for the projections for females. However, a slightly larger decrease in the lung cancer mortality rate for males was suggested by our model, which is a better fit to the observed data than the projections of Shibuya et al. Our study also confirmed that smoking prevalence is a poor measure of cumulative exposure to tobacco [7]. In addition, consistent with the results of another Australian study [3], we observed a slightly shorter lag between tobacco exposure and lung cancer mortality for males (26 years) compared to that for females (29 years). This is likely because lung cancer mortality is a function of cumulative tobacco exposure, and the level of smoking for females is generally lower than for males [3].

Cohort effects are considered to represent risk factors such as smoking behaviour that change from generation to generation [10, 18]. Consistent with previous studies, we confirmed that the cohort effect is a stronger predictor than the period effect for lung cancer mortality projections [6, 7, 30]. Birth cohort is suggested to be a better reflection of the number and type of cigarettes a cohort is exposed to when young [38], since smoking habits are generally established at an early age and are characteristic for a particular birth cohort [39]. Nevertheless, as our model has taken into account detailed data on cigarette consumption, the strong cohort effect is likely to also be reflecting changes in smoking habits other than cigarette tar exposure from generation to generation [40]. A previous study showed that cohort effects in lung cancer are dominated by the number of years smoked [18]. This is supported by the differences we observed in projected mortality rates for both males and females when applying an age-cohort model to earlier observed data without incorporating cigarette tar consumption, compared to our final model incorporating both birth cohort and cigarette tar consumption (Appendix 4). We speculate that the cohort effect may also reflect other cohort-specific smoking characteristics, such as the type of tobacco consumed, duration of smoking, and age of smoking initiation or cessation, as these characteristics are all related to birth cohort [18, 41]. In particular, the cessation of smoking can reduce the subsequent risk of lung cancer [42], and this is likely to be captured by the cohort effect as the population responds to tobacco control interventions over time.

This study has some limitations. The projections in this study involve uncertainties due to the variations in data quality between different smoking surveys. Age-specific tobacco consumption data were not available prior to 1972 and were backward estimated based on

the tobacco sales data and observed consumption data. In addition, data on average tar content per cigarette has not been collected in recent years due to uncertainty about the accuracy of the standard testing methods. Also, our projection models do not take into account other relevant factors which can be attributed to period effects, such as environmental and occupational factors, *ad hoc* lung cancer screening with low dose computerised tomography (for smokers – expected to be limited over the period of analysis), and changes in cancer treatment, including the introduction of epidermal growth factor receptor (EGFR) inhibitors. Previous research suggests that EGFR mutations are more common in patients who are non-smokers and patients from Asian backgrounds [43], although population level data on EGFR mutations and lung cancer mortality by ethnicity in Australia are not available. However, as it is estimated that only 12% of all non-small cell lung cancer patients in Australia have EGFR mutations [44], any potential future changes in the prevalence and survival patterns for that group should have limited impact on our projected estimates. Findings from a large scale cohort study in the USA reported that lung cancer mortality rates for non-smokers were stable [45], so we may expect a similar pattern in Australia over the period of analysis. Cancer screening and treatment factors were unlikely to be relevant for lung cancer mortality in the early years [30], and the relative survival rate has remained relatively stable over time [46]. Some other factors, such as duration of smoking and the age of smoking initiation, were not included in our models as the data are not available for early time periods. Fortunately, these smoking characteristics are likely to be captured by the cohort effect, as a previous study reported that the duration of smoking, age of smoking initiation and smoking cessation probabilities vary by birth cohort [18, 41]. Furthermore, the population denominators were themselves projected by the ABS [22, 23], and this adds some uncertainty to our projections.

Despite these limitations, this study also has many strengths. First, this study is based on long term observed data with high data quality and population coverage [20], and the data on deaths from cancer and recorded cause of death have been reported to be very complete and have been validated [47]. To ensure the data on smoking patterns are representative of the national population, where possible, we have restricted the smoking surveys to those conducted at a national level. Second, this is the first study to provide validation of projections for 25 years using observed data. Given the 26-29 years lag between tobacco exposure and lung cancer mortality, and with the observed tobacco consumption data being available until 2016, long term lung cancer mortality projections up to 2040 are likely to be reliable. Third, the present models have taken into account detailed data on the cigarette tar consumption by calendar period and birth cohort. Our model can be implemented using standard GLMs which are commonly available in statistical software packages. The advantages of these methods are that the lung cancer mortality rates are projected without making strong parametric assumptions to constrain period and cohort effects, and they allow the possibility of examining models that include more than one smoking-related variable. With the logarithmic link function, the cohort effects can be interpreted as relative risks relative to the reference cohort.

The projected decline in lung cancer mortality rates estimated by our study indicates that past and current tobacco control interventions implemented in Australia have been successful, resulting in continued reductions in lung cancer mortality. However, lung cancer mortality rates are still expected to remain at a relatively high level and the estimated increase in the actual number of deaths from lung cancer is still substantial. Given that, at a

population level, there is a lag of 26-29 years between smoking exposure and lung cancer mortality, the effects of newly implemented tobacco control programs may not have a significant impact on further reducing lung cancer mortality rates in the short term. This means that while the continued reduction in smoking prevalence remains a significant public health priority, it is also important that effective lung cancer screening and treatments are developed and implemented. Some recent positive developments in lung cancer screening and treatment include the validation of a lung cancer risk assessment tool to identify high risk individuals for targeted lung cancer screening in a large-scale population-based Australian cohort study [48], and that several randomized controlled trials in the USA and other countries have shown short term benefits of targeted therapy for lung cancer [49-51]. Although the cost-effectiveness of lung cancer screening compared to tobacco control programs is still inconclusive [52, 53], the potential benefits of both short and long term approaches to reducing lung cancer mortality should be explored.

We found that, not unexpectedly, incorporating tobacco consumption into our model considerably improves the accuracy of lung cancer mortality projections. Our best-fitting statistical model suggests that mortality rates for both males and females will continue to decline over the next 25 years in the context of the mature tobacco epidemic with past peaks in tobacco consumption for both males and females, with marked reductions in smoking prevalence and cigarette consumption for males since the 1950s and for females since the 1980s. However, the number of lung cancer deaths will continue to be substantial, and to increase, in Australia's ageing population. Our estimates of the number of deaths from lung cancer in Australia will inform planning to meet future health service needs and

these projected rates can serve as a benchmark against which to measure the effect of future lung cancer control initiatives in Australia.

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**Conflicts of interest statement**

None declared.

**Ethics approval and consent to participate**

Not applicable.

**Authorship contribution statement**

KC: conceived the study. QL: designed the study, conducted statistical analysis and interpretation, visualization, and drafted the manuscript with input from MC, SW, DO'C and KC. DO'C: contributed to the study design, interpretation of results and drafting of the manuscript. XQY: contributed to the study design. FP: contributed to the statistical analysis. All authors contributed to the interpretation of results and critically revised the manuscript. All authors read and approved the final manuscript.

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**Figure 1: Estimated smoking prevalence, annual number of cigarettes smoked per capita and annual cigarette tar exposure (g) by sex, age group and calendar year, Australia 1930-2020**

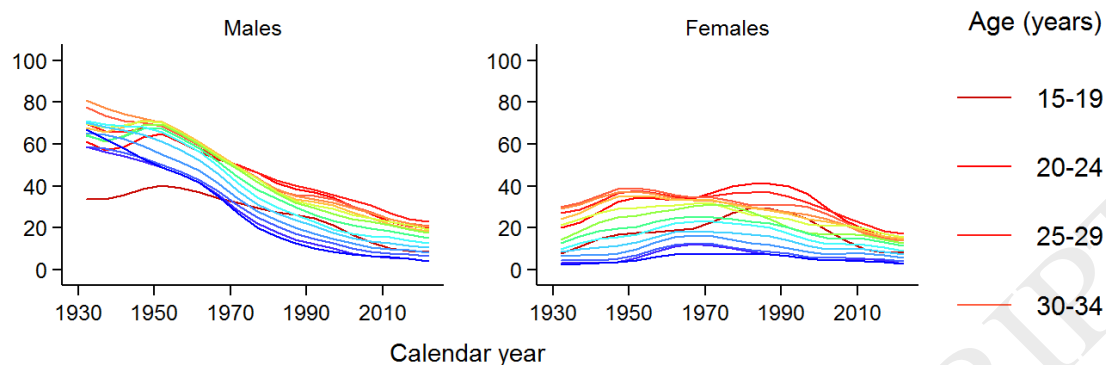
**Figure 2: Estimated prevalence of current smokers, annual number of cigarettes smoked, and annual cigarette tar exposure (g) per capita by sex, birth cohort and age group**

**Figure 3: Validation of 25-year projections using observed data for 1956-1990 projected to 2015, compared to observed data for 1956-2015**

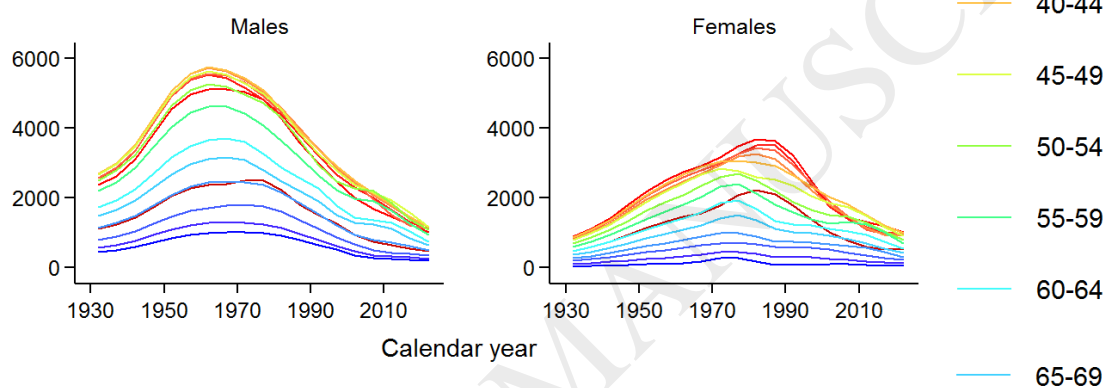
**Figure 4: Observed and predicted age-specific lung cancer mortality rates by age group, 1956-2040**

**Figure 5: Observed and projected numbers of deaths and age-standardized lung cancer mortality rates by sex, 1956-2040**

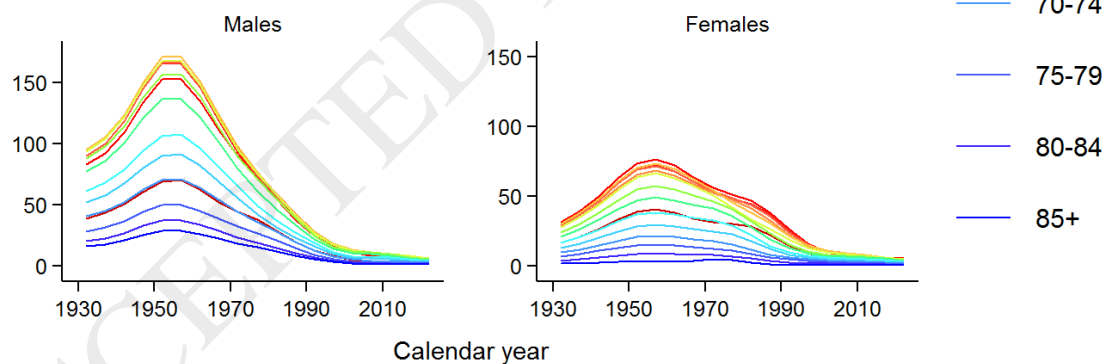
**A. Prevalence of current smokers %**



**B. Annual number of cigarettes smoked per capita**

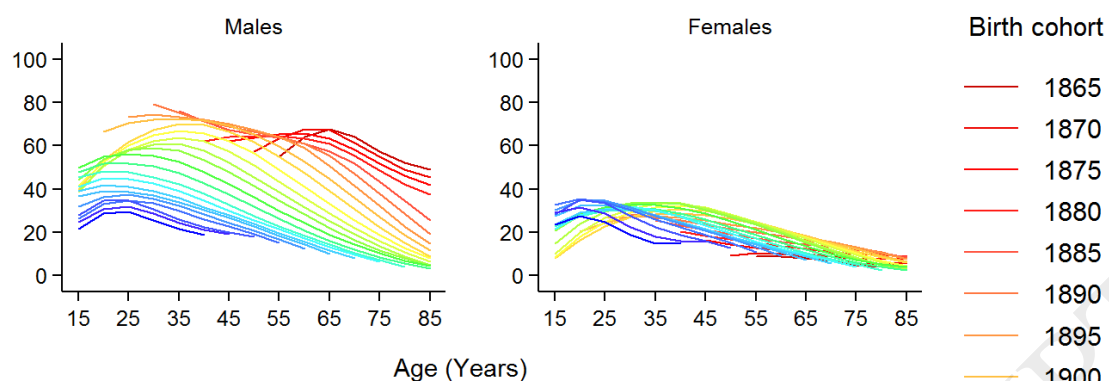


**C. Annual cigarette tar exposure (g) per capita**

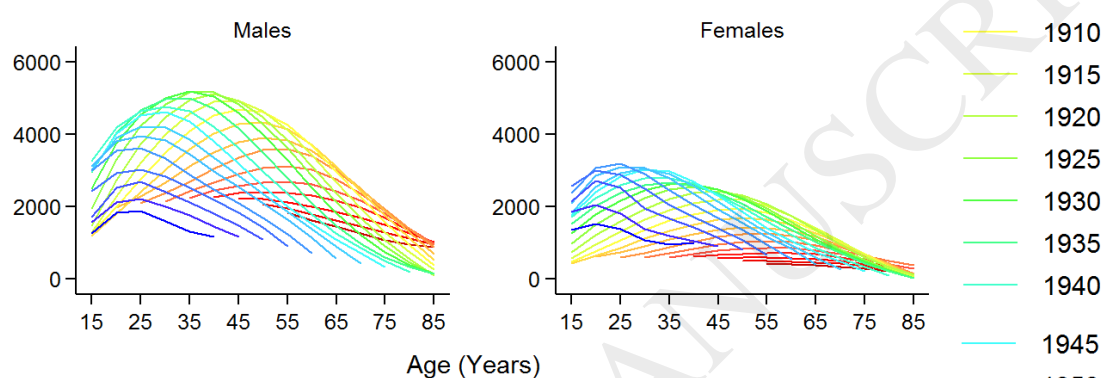




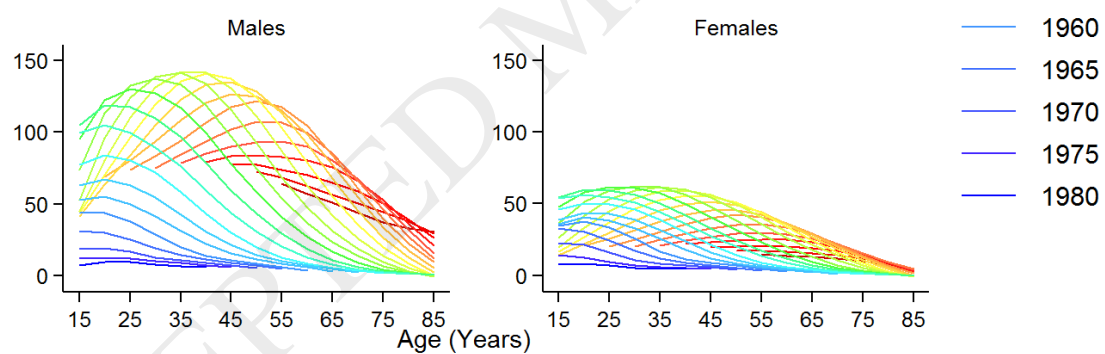
**A. Prevalence of current smokers %**

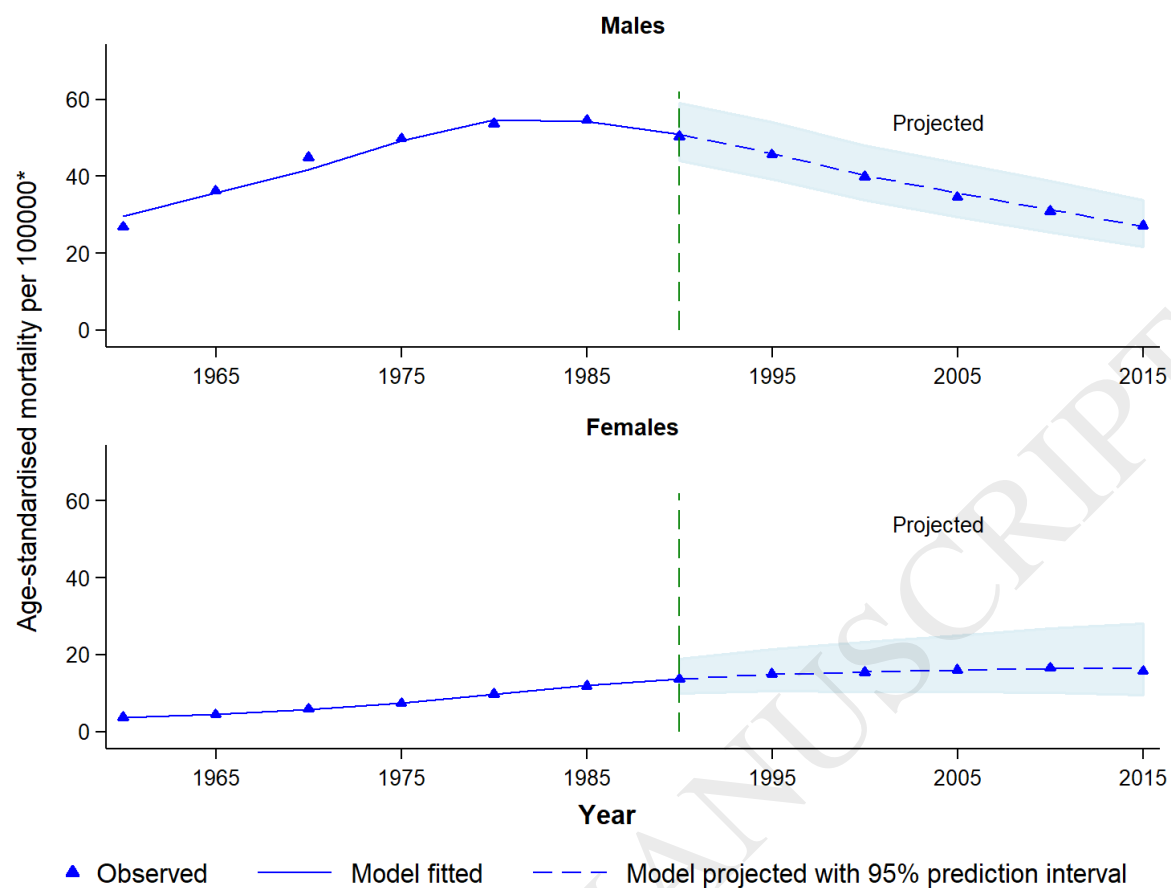


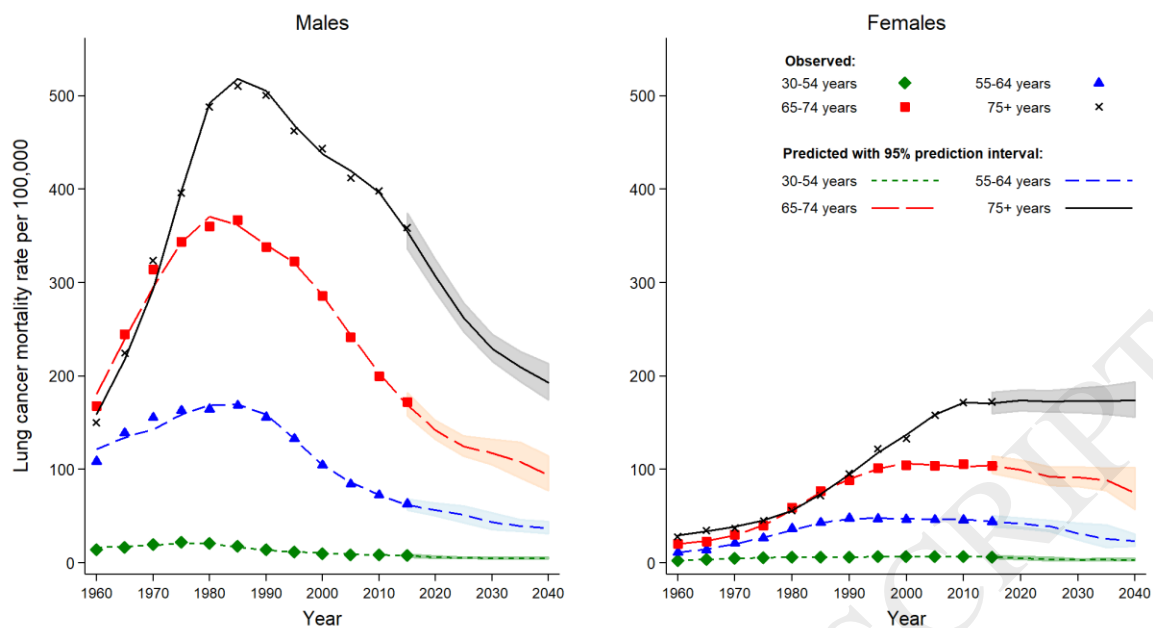
**B. Annual number of cigarettes smoked per capita**

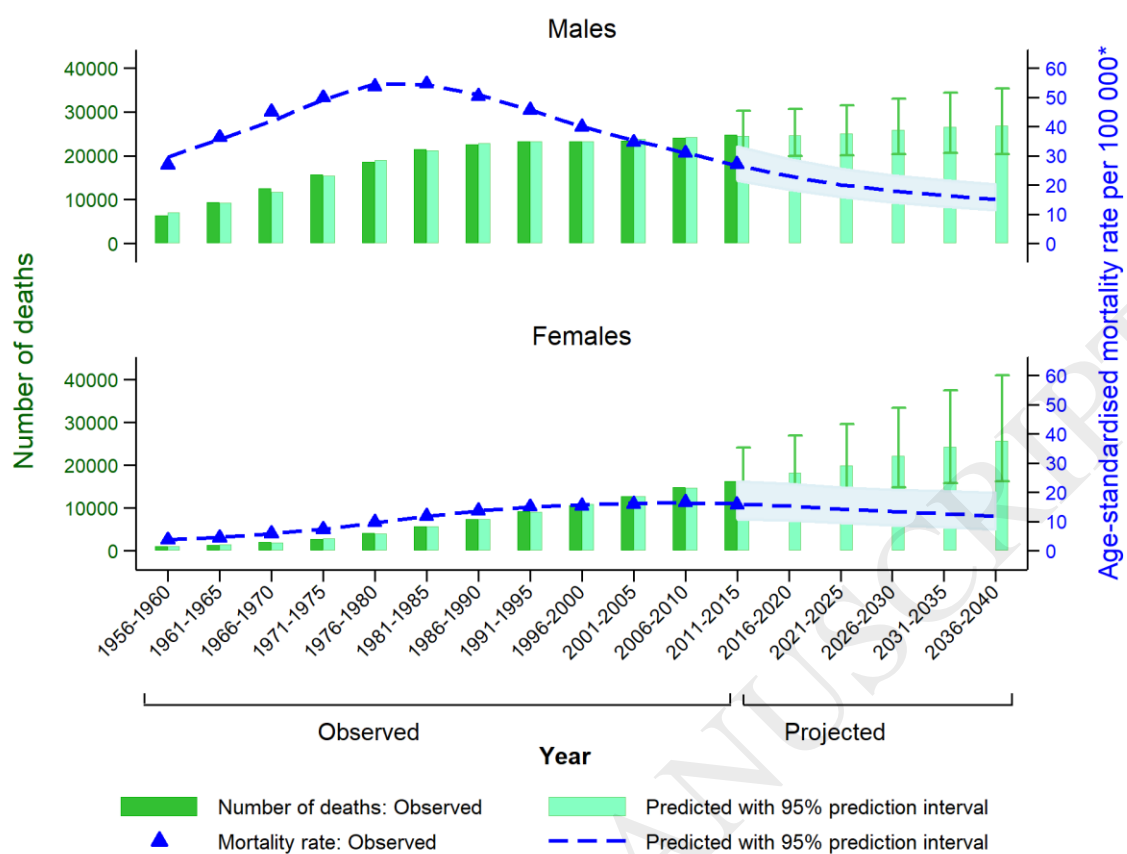


**C. Annual cigarette tar exposure (g) per capita**









**Table 1: Predicted and observed numbers of deaths from lung cancer and age-standardised lung cancer mortality rates\* by sex and 5-year period, 1956-2040**

Sex	Period	Number of deaths			Age-standardised mortality rate		
		Observed	Predicted (95% PI)		Observed	Predicted (95% PI)	
Male	1956-1960	6,384	7,037	(5,547 - 8,934)	26.9	29.6	(23.3 - 37.5)
	1961-1965	9,377	9,219	(7,277 - 11,684)	36.3	35.6	(28.1 - 45.2)
	1966-1970	12,580	11,697	(9,233 - 14,822)	45.0	41.8	(33.0 - 53.1)
	1971-1975	15,633	15,396	(12,079 - 19,625)	49.9	49.3	(38.6 - 62.9)
	1976-1980	18,628	18,959	(14,817 - 24,262)	53.7	54.6	(42.7 - 69.9)
	1981-1985	21,417	21,243	(16,697 - 27,028)	54.7	54.3	(42.7 - 69.0)
	1986-1990	22,606	22,791	(18,063 - 28,759)	50.5	50.9	(40.3 - 64.2)
	1991-1995	23,213	23,264	(18,616 - 29,075)	45.7	45.8	(36.6 - 57.3)
	1996-2000	23,251	23,250	(18,783 - 28,784)	40.0	40.0	(32.3 - 49.6)
	2001-2005	23,350	23,784	(19,290 - 29,337)	34.7	35.3	(28.6 - 43.6)
	2006-2010	24,128	24,176	(19,614 - 29,820)	30.9	31.0	(25.1 - 38.4)
	2011-2015	24,831	24,450	(19,812 - 30,208)	27.2	26.7	(21.6 - 33.2)
	2016-2020		24,686	(19,898 - 30,680)		23.0	(18.4 - 28.8)
	2021-2025		25,092	(20,034 - 31,502)		20.1	(15.9 - 25.6)
	2026-2030		25,877	(20,382 - 32,950)		18.0	(14.0 - 23.3)
	2031-2035		26,582	(20,596 - 34,416)		16.4	(12.5 - 21.7)
	2036-2040		26,805	(20,396 - 35,330)		15.1	(11.3 - 20.2)
<b>Total males 1956-2040</b>			<b>354,310</b>	<b>(281,134 - 447,216)</b>			
Sex	Period	Number of deaths			Age-standardised mortality rate		
		Observed	Predicted (95% PI)		Observed	Predicted (95% PI)	
Female	1956-1960	990	1,004	(689 - 1,466)	3.7	3.8	(2.6 - 5.5)
	1961-1965	1,336	1,381	(946 - 2,018)	4.5	4.6	(3.2 - 6.8)
	1966-1970	1,950	1,914	(1,312 - 2,793)	5.9	5.8	(4.0 - 8.5)
	1971-	2,769	2,779	(1,892 - 4,085)	7.4	7.4	(5.1 - 10.9)

1975						
1976-						
1980	4,111	3,995	(2,697 - 5,919)	9.8	9.5	(6.4 - 14.1)
1981-						
1985	5,645	5,598	(3,756 - 8,348)	11.9	11.8	(7.9 - 17.7)
1986-						
1990	7,359	7,330	(4,927 - 10,910)	13.7	13.6	(9.2 - 20.3)
1991-						
1995	9,178	9,099	(6,144 - 13,481)	15.1	15.0	(10.1 - 22.3)
1996-						
2000	10,581	10,818	(7,353 - 15,921)	15.4	15.7	(10.7 - 23.2)
2001-						
2005	12,638	12,750	(8,692 - 18,710)	16.1	16.2	(11.0 - 23.8)
2006-						
2010	14,770	14,613	(9,980 - 21,427)	16.6	16.3	(11.1 - 24.1)
2011-						
2015	16,209	16,403	(11,197 - 24,100)	15.8	16.0	(10.8 - 23.8)
2016-						
2020		18,192	(12,378 - 26,861)		15.3	(10.3 - 23.0)
2021-						
2025		19,913	(13,465 - 29,663)		14.3	(9.5 - 21.8)
2026-						
2030		22,097	(14,788 - 33,348)		13.4	(8.8 - 21.0)
2031-						
2035		24,184	(15,833 - 37,449)		12.7	(8.0 - 20.5)
2036-						
2040		25,598	(16,280 - 40,946)		11.8	(7.2 - 19.9)
<b>Total females</b>	<b>1956-2040</b>	<b>197,670</b>	<b>(132,330 - 297,443)</b>			

\*Age-standardised mortality rates are standardised to the WHO World Standard Population

PI: Prediction interval from bootstrap